Modern Concepts of Cardiovascular Disease

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JAUNDICE IN CONGESTIVE HEART FAILURE

Jaundice in congestive failure may be seen as often as it is assiduously looked for. This would imply that in many, indeed most, instances it is slight in degree. Nonetheless it is an important sign. Congestive heart failure is not only of common occurrence but it also causes serious secondary organismal disturbances of function, many of which further aggravate the general breakdown in the equilibrium and efficiency of the peripheral circulation. Thus a series of vicious circles are established which interact with each other and most of them conspire to embarrass still further cardiac efficiency.

The liver, due to its anatomical position in relation to the venous return flow to the heart, is after the lungs the most vulnerable organ to the circulatory disturbances of congestive heart failure. It must, however, be clearly understood that it is almost if not entirely affected by changes in venous pressure. There is no evidence to suggest that an increase in the arterial pressure as found in acute or chronic hypertension leads to liver damage. Even within the toxaemias of pregnancy when jaundice with hepatic necrosis and hypertension occur simultaneously one cannot be attributed to the other. On the contrary, there is every reason to believe that the jaundice which is the hepatic indicator of the hepatorenal syndrome which may follow traumatic shock is directly due to the liver damage consequent upon a prolonged period of low arterial pressure. In this case there is a relative ischemia which leads to degenerative anatomical lesions with impaired function which often is irreversible.

It is not with such conditions that we are at present concerned. It is well known that, along with the signs of pulmonary engorgement and oliguria, enlargement of the liver is considered an early and important index of congestive failure. It is also well known that the rapidity of progress of congestive failure varies considerably. In some instances, it may occur with explosive suddenness while in others the course is quite insidious, progressing to an advanced stage before the victim is completely incapacitated. This is in accordance with the course of events which result from disturbances of physiological function. It is presumed with fair reason that the more acute the disturbance the less time has the animal organism in which to marshall the powers of adaption to meet the new environment. This is applicable to both physiologic and anatomic changes.

As the pressure in the right ventricle increases and is progressively reflected into the right auricle and then into the vena cavae, the first organ to reveal this on physical examination is the liver through its enlargement. It is true that the keen observer may also note early dilatation or prominence of the jugular veins. But this may fluctuate so readily by posture that it is often overlooked. As the pressure continues to rise in the central hepatic veins, it is further reflected into their radicles until varying degrees of engorgement, edema and "cyanotic atrophy" develops.

If during this progression various tests to determine liver function are carried out there will be found a variable but definite impairment. Amongst these there will be found frequently an increase in the serum bilirubin. This may not be of sufficient degree to produce visible jaundice of the skin and conjunctivae. On the other hand, obvious jaundice is not unknown in tricuspid valvular insufficiency. Whereas it may occur where this is an acute derangement, it is more common in chronic stages of hepatic stasis. The cause of the jaundice was for some time in dispute, but now it is generally conceded to rest on a mechanical basis, the result of circulatory stasis and engorgement. This concept was originally put forward by Oertel[1-2-3] when he described a lesion which he called multiple non-inflammatory necrosis of the liver with jaundice in chronic cyanosis. He found that the process consisted of a multiple, irregular, circumscribed solution of the liver cells, without parenchymatous degeneration or coagulation necrosis, but associated with a corresponding blood and bile stasis. Keefer and Resnik[4-5] put forward the possibility that pulmonary infarction might play a role in the production of the jaundice in these cases by increasing the anoxia from an additional respiratory factor.

The character and relative proportion of the bilirubin in the blood throws an important side light on the causes of the jaundice in congestive failure. In pure obstructive jaundice, as for instance from occlusion of the common bile duct, the amount of water soluble bilirubin (direct Van den Bergh) amounts to 75 to 90 percent of the total (indirect Van den Bergh) which includes both water and alcohol soluble fractions. The 10 to 25 percent is therefore due to the alcohol fraction which is the precursor of hepatic bilirubin. This amount is more than is present under normal conditions and would indicate an impairment in hepatic function secondary to the biliary obstruction probably due to a purely mechanical effect.

In pure hemolytic jaundice, on the other hand, the amount of the water soluble fraction may only be 10 to 15 percent of the total which is largely composed of the precursor or alcohol soluble fraction. If, however, an obstructive factor be introduced as is common in familial hemolytic jaundice due to biliary

ANNUAL BUSINESS MEETING OF MEMBERS

The Annual Business Meeting of the Members of the American Heart Association will be held in Atlantic City, New Jersey, at 12 o'clock noon, June 4, 1949, in the Vernon Room of Haddon Hall, Chalfonte-Haddon Hall Hotel.

pigment thrombi in the biliary radicles or even in the hepatic or common ducts the ratio of the water soluble to the alcohol soluble fraction may increase to 40 to 50 percent of the total and variable amounts of bile pigment may be found in the urine. The predominance of the alcohol fraction under certain contions is usually attributed to one of two conditions (or both). These are, firstly, that the amount of the alcohol fraction of bilirubin being brought to the liver is greater than it can normally handle and so an excessive amount passes through it to the general circulation or, secondly, through impairment of hepatic function the Kupffer cells are not capable of handling the normal amount of the precursor of hepatic bilirubin brought to them so the pigment spills over to the general circulation. It might be expected that the amount of urobilinogen found in the urine might give a clue to which of these conditions were operative. Unfortunately this is not always the case. If it be taken that there is no obstructive biliary factor present there is an excessive amount of urobilinogen formed in the bowel in the first instance which is greater than the liver can normally handle and in the second instance, although the amount of the urobilinogen brought to the liver from the bowel may not be excessive, this function of handling it may be impaired and so an abnormal amount passes into the general circulation for excretion by the kidneys.

It would seem reasonable to accept, therefore, that there are two components in the production of jaundice in congestive circulatory failure. In the first instance the changes as described by Oertel are a constant finding at autopsy. These could quite obviously account for the presence of the water soluble fraction of the bilirubin in the blood and urine. These anatomical changes would also lead to severe local cellular anoxia in the liver and any additional anoxia from a pulmonary lesion could have an added effect. The wide spread destruction of the Kupffer cells and their impaired function from deficient blood supply and anoxia would be a potent factor in the permission of variable quantities of the precursor of bilirubin to pass through the liver and so explain the relatively large quantity of the alcohol soluble fraction found in the blood. In other words, there is both an obstructive factor and one of functional cellular deficiency present in these cases.

Although the presence of visible jaundice in congestive circulatory failure is of serious import, it is only so as it represents a severe degree of liver damage. It is practically always associated with present or past tricuspid insufficiency as indicated by pulsation of the liver with gross and usually painful enlargement and positive pulsation of the veins in the neck and even in the arms. If the equilibrium of the cardiac dynamics can be restored the jaundice will gradually disappear although there will be a time lag as the pigment is slowly removed from the cells of the skin and conjunctivae.

The distribution of the jaundice presents some interesting features. If the tricuspid valvular insufficiency be acute and edema is not prominent, the pigmentation will be fairly uniform through the skin. If, on the other hand, edema has been previously conspicuous then the jaundice will not appear in these areas. Furthermore the ascitic and pleural edema fluids if uncontaminated with blood will not contain bile pigments. The exact reason for the absence of the pigments in these fluids is not clear. It is suggested that whereas the pigmentation of the skin in jaundice is due to the deposition of the bile pigments in the cellular elements, rather than to its presence in the inter-cellular fluid, it continues to be concentrated in the former as the jaundice increases. Furthermore the diffusion of such a large molecule as that of bile pigments through the edematous tissues would be a difficult and slow process, particularly when the circulation rate is so retarded. There is every reason to believe that this retardation is greater in the lower than in the upper limbs. It is therefore not uncommon to find jaundice above the edema level and none below.[6]

An interesting side light is thrown on this aspect of the question by the following. Where giant urticaria occurs in a person with jaundice the pigmentation is much more intense in the urticarial areas. In such the permeability of the capillaries is increased and the local circulation of intercellular fluid accelerated. Both of these factors would tend to bring more pigment to the cells and thus the pigmentation would be intensified.

Jonathan Meakins, M.D.
Montreal, Canada

1. Oertel, H., Jour. Med. Res., 12:75:1904. Multiple Non-inflammatory Necrosis of the Liver with Jaundice.
2. Oertel, H., Jour. Exper. Med., 8:103:1906. A Further Contribution to the Knowledge of Multiple Non-Inflammatory Necrosis of the Liver with Jaundice. (Hepar necroticum cum Ictero) and to the Knowledge of Cell Degeneration and Cytolysis in General.
3. Oertel, H., Arch. Int. Med., 6:293:1910. Multiple Non-Inflammatory Necrosis of the Liver with Jaundice in Chronic Cyanosis.
4. Keefer, C. S., and Resnik, W. H., Jour. Clin. Invest., 2:375: 1926. Jaundice Following Pulmonary Infarction in Patients with Myocardial Insufficiency: I. A Clinical Study.
5. Resnik, W. H. and Keefer, C. S., Jour. Clin. Invest., 2:389: 1926. Jaundice Following Pulmonary Infarction in Patients with Myocardial Insufficiency: II. An Experimental Study.
6. Meakins, J. C., Jour. Clin. Invest., 4:1:1927. Distribution of Jaundice in Circulatory Failure.

ANNUAL DINNER

The Annual Dinner of the American Heart Association will be held in the Vernon Room, Chalfonte-Haddon Hall, Atlantic City, New Jersey, 7 p.m., Saturday, June 4, 1949. Members are invited to bring their family and friends. Application blank will be found at the bottom of page 39.

SECOND NATIONAL CONFERENCE OF EXECUTIVE SECRETARIES

The second National Conference of Executive Secretaries of the American Heart Association will take place on Thursday, June 2, 1949, from 9:30 a.m. to 5 p.m., in the Viking Room of Haddon Hall, and Friday, June 3, 1949, from 9:30 a.m. to 12 noon, in the Rutland Room of Haddon Hall, Chalfonte-Haddon Hall Hotel, Atlantic City, New Jersey.

PROGRAM
TWENTY-SECOND SCIENTIFIC SESSIONS
AMERICAN HEART ASSOCIATION
June 3-4, 1949
Vernon Room, Haddon Hall, Atlantic City, N. J.

FIRST SESSION
1:30 P.M., Friday, June 3

Chairman: Norman E. Freeman, Chairman, Section on Circulation
Secretary: Grace M. Roth

1. THE EFFECTS OF DIHYDROERGOCORNINE ON THE CEREBRAL CIRCULATION OF HYPERTENSIVE AND NORMOTENSIVE SUBJECTS.
   Joseph H. Hafkenschiel, Charles W. Crumpton, John H. Moyer, and William A. Jeffers, Philadelphia, Pennsylvania.
2. SYMPATHETIC VENOCONSTRICTOR REFLEXES IN MAN.
   Julius Litter and Robert W. Wilkins, Boston, Massachusetts.
3. STUDIES OF THE PULMONARY AND SYSTEMIC ARTERIAL PRESSURE IN CASES OF PATENT DUCTUS ARTERIOSUS WITH SPECIAL REFERENCE TO EFFECTS OF SURGICAL LIGATION.
   B. E. Taylor, A. A. Pollack, H. B. Burchell, O. T. Clagett, and E. H. Wood, Rochester, Minnesota.
4. GEORGE BROWN MEMORIAL LECTURE — BLOOD COAGULATION AND THE PRACTICAL SIGNIFICANCE OF RECENT ADVANCES IN OUR KNOWLEDGE OF PROTHROMBIN AND Ac-GLOBULIN.
   Walter H. Seegers, Wayne University College of Medicine, Detroit, Michigan.
5. SYNTHETIC RATIONS IN THE STUDY OF DIETARY FACTORS IN EXPERIMENTAL RENAL HYPERTENSION IN THE RAT.
   Philip Handler and F. Bernheim, Durham, North Carolina.
6. ARTERIOSCLEROSIS AND PYRIDOXINE DEFICIENCY.
   J. F. Rinehart and L. D. Greenberg, San Francisco, California.
7. RELATIONSHIP BETWEEN PROTHROMBIN TIME AND PLASMA LEVELS OF DICOUMAROL.
   Murray Weiner, Shepard Shapiro, Julius Axelrod, and Bernard B. Brodie, New York, New York.
8. EPINEPHRINE AND NOR-EPINEPHRINE IN PHEOCHROMOCYTOMA.
   Marcel Goldenberg and Henry Aranow, Jr., New York, New York.
9. HEPATO-RENAL VASOTROPIC FACTORS IN ESSENTIAL HYPERTENSION AND IN ECLAMPSIA.
   Ephraim Shorr and Benjamin W. Zweifach, New York, New York.
10. THE MECHANISM OF SOME ANTIDIURETIC RESPONSES AND THEIR RELATIONSHIP TO THE SODIUM RETENTION OF CONGESTIVE CARDIAC FAILURE.
    B. C. Sinclair-Smith, J. H. Sisson, A. Genecin, A. Kattus, C. Monge, and E. V. Newman, Baltimore, Maryland.
11. THE EFFECT OF DIGOXIN IN LEFT VENTRICULAR FAILURE.
    M. Irene Ferrer, Rejane M. Harvey, Richard T. Cathcart, Andre Cournand, and Dickinson W. Richards, Jr., New York, New York.

SECOND SESSION
9:00 A.M., Saturday, June 4

Chairman: Tinsley R. Harrison, President, American Heart Association
Secretary: John J. Sampson

12. THE TREATMENT OF COARCTATION OF THE AORTA.
    Robert E. Gross, Boston, Massachusetts.

I enclose $.....for.....reservations at $6.50 each for the Annual Dinner of the Association, to be held at the Chalfonte-Haddon Hall, Atlantic City, N. J., on Saturday, June 4, 1949.

Name.....

Street and Number.....

City and State.....

(Please make checks payable to American Heart Association, Inc.)

13. COMMISSUROTOMY FOR MITRAL STENOSIS.
Charles P. Bailey, Robert P. Glover, and Thomas J. O'Neill, Philadelphia, Pennsylvania.

14. THE NATURE AND TREATMENT OF AURICULAR FLUTTER.
Myron Prinzmetal, Eliot Corday, Alvin L. Sellers, Walter A. Flieg, and H. E. Kruger, Los Angeles, California.

15. CATHETERIZATION OF THE LEFT HEART IN MAN.
Henry A. Zimmerman, Roy W. Scott, and Norman O. Becker, Cleveland, Ohio.

16. THE VECTORAL INTERPRETATION OF PRECORDIAL T-WAVE INVERSION.
Robert P. Grant, Atlanta, Georgia.

17. QRS-T PATTERNS IN THE PRECORDIAL LEADS THAT MAY BE MISTAKEN FOR MYOCARDIAL INFARCTION.
Gordon B. Myers, Detroit, Michigan.

18. THE SYNDROME OF ACUTE MYOCARDIAL INFARCTION ASSOCIATED WITH EARLY ELECTROCARDIOGRAPHIC FINDINGS SUGGESTIVE OF PREDOMINANTLY SUBENDOCARDIAL INJURY, WITH OBSERVATIONS ON THE "TOUCH EFFECT" OF THE CARDIAC CATHETER.
Hans H. Hecht, Leonard W. Ritzmann, and Marguerite Greaves, Salt Lake City, Utah.

19. THE SUBCUTANEOUS USE OF THIOMERIN, A NEW MERCURIAL DIURETIC FOR TREATMENT OF CONGESTIVE HEART FAILURE.
Robert C. Batterman, David Unterman, and Arthur C. De Graff, New York, New York.

12:00 P.M., Saturday, June 4

ANNUAL BUSINESS MEETING OF MEMBERS.

THIRD SESSION

Saturday, June 4

Panel Discussions

Chairman: Eugene A. Stead, Jr., Chairman, Program Committee

1:30 P.M. — 2:30 P.M.

1. MANAGEMENT OF CONGESTIVE FAILURE AND IMPORTANCE OF LOW SODIUM DIET.
George E. Burch, New Orleans, Chairman
William Dock, New York
Walter Kempner, Durham
Samuel Proger, Boston
Ferdinand Schemm, Great Falls
James Warren, Atlanta

2:35 P.M. — 3:35 P.M.

2. CONGENITAL HEART DISEASE.
Alfred Blalock, Baltimore, Chairman
Richard Bing, Baltimore
Louis E. Martin, Los Angeles
Edward Neuhauser, Boston
Helen Taussig, Baltimore

3:40 P.M. — 4:40 P.M.

3. ANTICOAGULANT THERAPY.
Edgar V. Allen, Rochester, Chairman
Louis N. Katz, Chicago
I. S. Ravdin, Philadelphia
Walter H. Seegers, Detroit
Geza de Takats, Chicago
Irving S. Wright, New York

You are invited to forward a question or topic which you would like to have discussed at any of these panels to the American Heart Association, 1775 Broadway, New York 19, N. Y.

7:00 P.M., Saturday, June 4

Annual Dinner

Vernon Room, Haddon Hall

PROGRAM COMMITTEE

Chairman, Eugene A. Stead, Jr., Durham

Graham Asher, Kansas City
James A. Greene, Houston
John Hepburn, Toronto
Louis N. Katz, Chicago
Robert L. King, Seattle
William G. Leaman, Jr., Philadelphia
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Roy W. Scott, Cleveland
Arthur P. Selzer, San Francisco
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